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BUTZEL LONG
IP DOCKETING DEPT
350 SOUTH MAIN STREET
SUITE 300
ANN ARBOR, MI 48104

EXAMINER	
SCHUBERG, LAURA J	
ART UNIT	PAPER NUMBER
1657	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATENT@BUTZEL.COM
BOUDRIE@BUTZEL.COM

Office Action Summary	Application No.	Applicant(s)	
	10/549,987	CHEN ET AL.	
	Examiner	Art Unit	
	LAURA SCHUBERG	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is responsive to papers filed 07/21/2008.

Claims 1 and 6 have been amended and no claims have been canceled or newly added.

Claims 1-18 are currently pending and have been examined on the merits.

Response to Arguments

Applicant's arguments filed 07/21/2008 have been fully considered but they are not persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Applicant argues that because the Yatvin reference requires the presence of a polycyclic aromatic antioxidant that one of skill in the art would not have been motivated to combine the Coenzyme Q10 in the liposome composition of Keller and the ceramide of the preliposomal composition of Yatvin to obtain the CoQ10-containing preliposomes of Applicant's claim 1. Applicant asserts that the teachings of Yatvin exclude Coenzyme Q10.

This is not found persuasive because the teachings of Yatvin are directed to a medical composition for the treatment of heart disease wherein the active agent is an antioxidant. One of ordinary skill in the art would have been sufficiently motivated to enhance the composition of Yatvin with additional antioxidents, especially those known

in the art to be beneficial for the treatment of heart disease as well (such as Coenzyme Q10). Yatvin also teaches that additional advantageous components comprise the composition and will be understood by those with skill in the art (column 5 lines 44-47). Clearly Yatvin does not exclude the addition of Coenzyme Q10 or any other ingredient known to be beneficial to a patient.

Applicant argues that Keller actually discloses a liposome composition and not a proliposomal composition. Applicant asserts that while Keller may mention a preliposomal formulation it cannot be said that such a formulation is taught because these formulations are not prepared in any of the examples by Keller.

This is not found persuasive because patents are relevant as prior art for all they contain. "The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983). A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). Nonpreferred embodiments constitute prior art. Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 27 F.3d 551,

554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). See M.P.E.P. §2123. Clearly Keller indicates that Coenzyme Q10 is a suitable biologically active material for incorporation into a preliposomal formulation.

Applicant argues that the claimed invention provides unexpected stability of Coenzyme Q10. Applicant asserts that the spongiamine contained in the CoQ10-containing preliposomes can further facilitate the percutaneous absorption and improve the effect of CoQ10 in cosmetic formulations.

This is not found persuasive because Yatvin teaches that proliposomal formulations are expected to improve stability of compositions (column 4 lines 45-52). Wen-Jian Lan et al. teach that ceramides are highly effective for moisturizing (page 2 of translation) and include Spongiamine A and Spongiamine B (abstract and Page 3 of translation). The data of Wen-Jian Lan shows that spongiamine are characterized by the classical structure of ceramides (page 4 of translation). Therefore, spongiamine would be expected to provide comparable moisturizing and percutaneous absorption benefits that other ceramides do.

In submitting evidence asserted to establish unobvious results, there is a burden on an applicant to indicate how the examples asserted to represent the claimed invention are considered to relate to the examples intended to represent the prior art and, particularly, to indicate how those latter examples do represent the closest prior art. See *In re Borkowski*, 595 F.2d 713, 184 USPQ 29 (CCPA 1974); *In re Goodman*, 339 F.2d 228, 144 USPQ 30 (CCPA 1964).

The evidence relied upon should also be reasonably commensurate in scope with the subject matter claimed and illustrate the claimed subject matter "as a class" relative to the prior art subject matter "as a class." *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971); *In re Hostettler*, 429 F.2d 464, 166 USPQ 558 (CCPA 1970). See, also, *In re Lindner*, 457 F.2d 506, 173 USPQ 356 (CCPA 1972).

It should also be established that the differences in the results are in fact unexpected and unobvious and of both statistical and practical significance. *In re Merck*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986); *In re Longi*, 759 F. 2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Klosak*, 455 F2d 1077, 173 UAPQ 14 (CCPA 1972); *In re D'Ancicco*, 429 F.2d 1244, 169 USPQ 303 (CCPA 1971). *Ex parte Gelles*, 22 USPQ2d 1318 (BPAI 1992).

Priority

Receipt is acknowledged of papers filed under 35 U.S.C. 119 (a)-(d) based on an application filed in China on 03/20/2003. Applicant has complied with the requirements of 37 CFR 1.63(c), since the oath, declaration or application data sheet does acknowledge the filing of the foreign application.

The current amendment to the specification filed 07/21/2008 has the incorrect date of the Chinese Priority Patent as March 3, 2003. The correct date is March 20, 2003.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-8, 10, 12-18 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Yatvin (US 6,824,790) in view of Keller (US 2002/0039595) and Wen-Jian Lan, et al. (Acta Scientarium Naturalium Universitatis Sunyatseni ,Jan. 2004).

Amended claim 1 is drawn to CoQ10- containing preliposomes, which contain spongiamine in liposome structures pf the CoQ10-containing preliposomes.

Dependent claims include wherein the preliposomes are a granular, lyophilized solid; concentrations of CoQ10; additional lipid components and formulation as a pharmaceutical.

Amended claim 6 is drawn to a method of preparing the CoQ10-containing preliposomes of claim 1 which comprises: preparing a lipid solution by one of a) melting CoQ10 and spongiamine; and b) dissolving CoQ10 and spongiamine in an organic solvent; and applying the lipid solution to an underlay to produce the CoQ10-containing preliposomes which contain spongiamine.

Dependent claims include the composition of the underlay; wherein the lipid solution is applied to the underlay by one of several methods; wherein the resulting mixture is subject to at least one of several drying methods and the composition of the underlay.

Yatvin teaches pharmaceutical compositions and methods of making wherein the proliposomal compositions include an antioxidant (column 7 lines 16-35), a ceramide and cholesterol (column 7 lines 5-10). Wherein the composition is in dry granular form (column 6 lines 22-32) lyophilized and then compressed into a solid tablet is taught (column 9 lines15-20). The presence of the cholesterol lowers the melting point of the lipid solution so that a lower temperature may be used to melt the antioxidant and lipid (ceramide) (column 10 lines 31-43). The use of lactose in the method is taught as well as dissolving the components with an organic solvent (column 7 lines 58-column 8 line 2 and column 8 lines 49-column 9 line 9). Yatvin suggests that one intended use of the composition is to treat coronary artery and heart disease (column 1). Additional

advantageous components comprise the composition and will be understood by those with skill in the art (column 5 lines 44-47). Yatvin also teaches that modifications or alternatives equivalent thereto are within the spirit and scope of the invention (column 13 lines 57-62).

Yatvin does not specifically teach including coenzyme Q10 as the antioxidant or spongiamine as the ceramide.

Keller teaches a method of making a preliposome formulation and then dehydrating it. Biologically active materials for the preliposomal formulation include nutritional supplements and antioxidants such as coenzyme Q10 (page 4 claim 5). The concentration of CoQ10 is indicated in example 2 as 1.29 % (page 3). Ceramides and sphingolipids are taught as suitable as the lipid component (page 2 para 16). Cholesterol is taught as added to the preliposome formulation (page 2 para 16). Liposomal formulations with ceramides are taught to increase bioavailability of an antioxidant which is poorly absorbed orally (page 1 para 10-page 2).

Wen-Jian Lan et al. teach the discovery of two new ceramides named Spongiamine A and Spongiamine B that were isolated from the sponge *Spongia* sp. (abstract and page 3 of translation). Ceramides are taught to be the main structure for forming sphingolipids and offer advanced activity in anti-tumor, anti-virus, anti-hepatotoxic and immunization uses as well as highly effective for moisturizing (page 2 of translation). The data show that spongiamine are characterized by the classical structure of ceramides (page 4 of translation).

Applicant's disclosure teaches that methods such as a membrane dispersion method or a melt method or an infuse method to obtain CoQ10-containing liposomes which contain the underlay are known in the prior art (page 4 lines 11-14).

Therefore, one of ordinary skill in the art would have been motivated to include CoQ10 in the method and composition of Yatvin as an antioxidant because Keller teaches that CoQ10 is a suitable antioxidant to be used in a preliposomal formulation. One of ordinary skill in the art would have had a reasonable expectation of success because Yatvin teaches that proliposomes are ideally suited for lipophilic compounds and have implications for developing formulations that stabilize encapsulated drugs (page 8 para 97). The concentration of CoQ10 taught by Keller of 1.29% falls in the same ranges as claimed by Applicant.

One of ordinary skill in the art would have been motivated to include the ceramide spongiamine in the method of Yatvin because Wen-Jian Lan et al. teach the discovery of two new ceramides named Spongiamine A and Spongiamine B that were isolated from the sponge *Spongia* sp. (abstract and page 3 of translation) and have numerous benefits (page 2 of translation). One of ordinary skill in the art would have had a reasonable expectation of success because Wen-Jian Lan et al. teach that spongiamine are characterized by the classical structure of ceramides (page 4 of translation); are the main structure for forming sphingolipids; and Keller teaches that sphingolipids as well as ceramides are also suitable as the lipid component of a preliposome (page 2 para 16).

One of ordinary skill in the art would have been motivated with a reasonable expectation of success of using the methods of membrane dispersion method or a melt method or an infuse method to obtain CoQ10-containing liposomes which contain the underlay since they are known methods in the prior art as disclosed by Applicant.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Therefore, the combined teachings of Yatvin, Keller, and Wen-Jian Lan, et al. render obvious Applicant's invention as claimed.

Claim 9 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Yatvin (US 6,824,790) in view of Keller (US 2002/0039595) and Wen-Jian Lan, et al. (Acta Scientarium Naturalium Universitatis Sunyatseni ,Jan. 2004) as applied to claims 1-8, 10 and 12-18 above, and further in view of Hoppe et al. (US 6,261,575).

Claim 9 includes formulating the composition of claim 1 as a cosmetic.

The combined teachings of Yatvin, Keller, and Wen-Jian Lan, et al. render obvious claim 1 as described above, but do not mention formulating the composition as a cosmetic.

Hoppe et al. teach a cosmetic formulation of a composition that contains 0.05-1 % CoQ10 and cholesterol (column 4, lines 35-45). The reference also teaches that it is

advantageous to add ceramides to the formulations (column 5 lines 45-48) and that they can be encapsulated in liposomes with ceramides as well (column 6 lines 24-28).

Therefore, one of ordinary skill in the art would have been motivated to incorporate the preliposomal formulations of Yatvin containing CoQ10 and ceramides into cosmetic formulations because Hoppe et al. teach that these ingredients are advantageous for cosmetic skin care products. One of ordinary skill in the art would have been motivated to add spongiamine as the ceramide because Wen-Jian Lan et al. teach that ceramides such as spongiamine offer advanced activity in anti-tumor, anti-virus, anti-hepatotoxic and immunization uses as well as highly effective for moisturizing (page 2 of translation). One of ordinary skill in the art would have had a reasonable expectation of success because Keller teaches that compositions containing CoQ10 in liposomal format can be administered topically as well as orally (page 2 para 15).

Therefore, the combined teachings of Yatvin, Keller, Wen-Jian Lan, et al., and Hoppe et al. render obvious Applicant's invention as claimed.

Claim 11 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Yatvin (US 6,824,790) in view of Keller (US 2002/0039595) and Wen-Jian Lan, et al. (Acta Scientarium Naturalium Universitatis Sunyatseni ,Jan. 2004) as applied to claims 1-8, 10 and 12-18 above, and further in view of Chen et al. (Journal of Pharmaceutical Sciences, 1987) and Weithmann et al. (US 5,318,987).

Claim 11 is drawn to the method of claim 6 wherein the lipid solution is applied to the underlay using a fluidized bed and the organic solvent is evaporated in the fluidized bed.

The combined teachings of Yatvin, Keller, and Wen-Jian Lan, et al. render obvious claim 6 as described above, but do not specifically mention using a fluidized bed.

Chen et al. teach that use of a fluidized bed is advantagous for formulating proliposomes because 1) the film coating technology using the fluidized bed is well established and processable; 2) various cores and coating materials are available or easy to prepare; and 3) it is cost effective to prepare liposomes for drug delivery by oral and/or many other routes of administration (page 1, last paragraph).

Weissman et al. teach a method of preparing antioxidant/lipid solutions in a liposomal formulation using a fluidized bed to form tablets that contain carriers such as various sugars (lactose) (column 11-column 12). Weissman et al. also teach that better results are obtained if the lipophilic antioxidants are additionally incorporated during the preparation of liposomes as components thereof (column 51 lines 44-46). These formulations can be used in pharmaceuticals as well as cosmetics (column 9 lines 34-40).

Therefore, one of ordinary skill in the art would have been motivated to use the fluidized bed technology in the method of Yatvin to form the preliposomal composition because of the advantageous taught by Chen et al. above. One of ordinary skill in the art would have had a reasonable expectation of success because Weissman et al.

teach that fluidized bed technology has been successfully used to form liposomal formulations with lipophilic antioxidants and CoQ10 is a lipophilic antioxidant.

Therefore, the combined teachings of Yatvin, Keller, Wen-Jian Lan, et al., Chen et al. and Weithmann et al. render obvious Applicant's invention as claimed.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA SCHUBERG whose telephone number is (571)272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

Laura Schuberg